REMARKS

Applicants respectfully request consideration of the foregoing amendments and the following comments upon continued examination of the present application.

I. Status of the Claims

Claims 1-26, 51-53 and 107-109 were cancelled previously. Claim 27 has been amended to add the recitation of "anti-inflammatory agents" and "antibiotics," with exemplary support in the original claims. Claims 27-50 read on the elected invention. Claim 87 has been amended to delete the negative proviso.

Because no new matter is introduced, Applicants respectfully request entry of this amendment. Upon entry, claims 27-50 and 87-106 are under examination, with claims 54-86 and 110-111 withdrawn from consideration.

II. Rejection of Claims under 35 U.S.C. §112, first paragraph

Claims 87-106 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of written description. Office Action at page 2-3. Applicants respectfully traverse the rejection.

The Examiner contends that the specification does not provide sufficient support for the negative limitation "wherein the active agent is not a non-steroidal anti-inflammatory drug." Without acquiescing to the stated basis of the rejection, Applicants choose to advance prosecution by deleting the phrase in question, thereby mooting the ground of the rejection.

III. Rejection of Claims under 35 U.S.C. §102(b)

Claims 87-93 and 96-105 are rejected under 35 U.S.C. §102(b) for alleged anticipation by U.S. Patent No. 5,518,738 to Eickhoff et al. ("Eickhoff"). Office Action at pages 3-6. Applicants respectfully traverse the rejection.

As submitted in the prior responses, Eickhoff fails to meet the claim limitations of (1) "a solid dose matrix surrounding the nanoparticulate active agent and at least one surface stabilizer" and (2) "the solid dose matrix disintegrating or dissolving upon contact with saliva in less than about 3 minutes."

The Examiner asserts that the disintegration profile of the solid dose matrix of the claimed invention is an "inherent" property of Eickhoff's composition. However, the rejection is based on an improper reliance on the "inherency" doctrine. MPEP 2112 sets forth that the Examiner may invoke "inherency" if it can be established that the prior-art product is substantially identical to the claimed invention. Eickhoff fails to teach a solid dose matrix to meet Applicants' claim limitation, as detailed below, and therefore the composition of Eickhoff is not "substantially identical" to that of the claimed invention.

The Examiner contends that "the instant solid dose matrix. . . is construed to mean any solid dose form containing the same components" (final Office Action, page 14, last paragraph). Applicants respectfully disagree with the Examiner's construction of the claim language. As disclosed in the specification, the claimed invention successfully obtains "a solid, porous, rapidly disintegrating solid oral dosage form having the active ingredient distributed throughout" (page 15, lines 23-25).

To attest to this point, Applicants further submit herewith a declaration executed by Dr. Stephen Ruddy. A solid dose matrix is shown as a porous matrix surrounding the active agent particles. *See* Ruddy Declaration, section 5. Upon contact with saliva, the excipients forming

the solid dose matrix are anticipated to rapidly hydrate and dissolve or swell, thereby resulting in rapid disintegration of the solid dosage form. *Id*, section 6.

Accordingly, the Examiner's rejection based on incorrect construction of the claim language should be withdrawn.

IV. Rejection of Claims under 35 U.S.C. §103(a)

A. Eickhoff, Specification and Allen

Claims 87-106 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Eickhoff in view of the specification (page 1, line 31 through page 4, line 22) or U.S. Patent No. 6,177,104 to Allen et al. ("Allen"). Office Action at pages 6-8. Applicants respectfully traverse the rejection.

The teaching of Eickhoff is discussed in the foregoing paragraphs. Contrary to the Examiner's assertion that there was "routine knowledge in preparing micro- or nano-particulate compositions in a rapidly disintegrating or dissolving solid oral dose or matrix form" (final Office Action, page 7, lines 11-12), the specification explicitly discloses that as of the priority date for the present application a fast-melt dosage form was **NOT** available in a nanoparticulate active agent form. An excerpt of the specification at page 4, lines 23-32 is reproduced below:

> None of the described prior art teaches a rapidly disintegrating or dissolving, or "fast melt," dosage form in which a poorly soluble active ingredient is in a nanoparticulate form. This is significant because the prior art fast melt formulations do not address the problems associated with the bioavailability of poorly soluble drugs. While prior art fast melt dosage forms may provide rapid presentation of a drug, frequently there is an undesirable lag in the onset of therapeutic action because of the poor solubility and associated slow dissolution rate of the drug. Thus, while prior art fast melt dosage forms may exhibit rapid disintegration of the drug carrier matrix, this does not result in rapid dissolution and absorption of the poorly soluble drug contained within the dosage form.

Allen relates to a particulate support matrix for making a rapidly dissolving dosage form but fails to disclose the oral solid dose rapidly disintegrating nanoparticulate active agent formulation of the claimed invention. The Examiner makes reference to Allen, at column 2, lines 30-31 and column 3, lines 57-58, for the alleged teaching of "routine knowledge in preparing. . . nano-particulate compositions." However, the Examiner's assertion is based on a misinterpretation of Allen's teaching.

The relevant text quoted by the Examiner discloses that "[t]o effectively mask the taste of poorly tasting drugs, it is generally necessary to micro-encapsulate or nano-encapsulate them." As illustrated by the diagram of Exhibit A (http://www.gmdbioadvance.net/technology_creation.html), a nano-encapsulation process is irrelevant to Applicants' claimed compositions comprising a nanoparticulate active agent having an effective average particle size of less than about 2000 nm. Rather, a nano-encapsulation process entails multiple coatings by oppositely charged polyelectrolytes to encapsulate a core having a size of between 200 nm and 50 μm.

Moreover, a reason to combine the teachings of Eickhoff and Allen is lacking. Eickhoff explicitly discloses that it is required to combine hygroscopic sugar and sodium lauryl sulfate to achieve the "synergistic" effect and that "addition of hygroscopic sugar or sodium lauryl sulfate alone is not sufficient to redisperse the solid nanonaproxen in gastric fluid to a great extent" (column 6, lines 43-48). Allen requires the presence of at least two polymeric components, e.g., polypeptide components having the same sign of net charge, to form the dosage form matrix (abstract and claim 1). As such, it is impossible for one skilled in the art to combine the teachings of the cited references because they are directed to different approaches.

B. Eickhoff, Specification, Allen and Kerkhof

Claims 87-106 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Eickhoff, the specification, Allen, and further in view of PCT Publication No. WO 01/45674 by Kerkhof et al. ("Kerkhof"). Office Action at pages 8-11. Applicants respectfully traverse the rejection.

The teachings of Eickhoff, the specification and Allen are discussed supra. Kerkhof is cited for the alleged teaching of nanoparticulate compositions comprisings nonsoluble drugs, such as anti-inflammatory agents including NSAIDs, such as indomethancin, naproxen and ketoprofen, antibiotics, etc. *See* final Office Action, page 9, lines 1-3. However, Kerkhof does not compensate for any deficiencies of the primary and secondary references as discussed above. Specifically, Kerkhof does not teach or suggest an rapidly disintegrating oral solid dose comprising a nanoparticulate active agent composition and a solid dose matrix surrounding the nanoparticulate active agent composition.

In view of the foregoing, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103(a).

V. Double Patenting Rejection

A. U.S. Patent No. 6,316,029

Claims 87-106 are rejected for alleged obviousness type double patenting over claims 1-24 and 51-70 of U.S. Patent No. 6,316,029. Office Action at page 11. Applicants choose to defer any action until the Examiner indicates that the pending claims are allowable otherwise.

B. U.S. Patent No. 6,165,506

Claims 87-106 are rejected for alleged obviousness type double patenting over claims 1-16 and 21 of U.S. Patent No. 6,165,506 ("the '506 patent"), further in view of Applicants'

allegedly admitted prior art. Office Action at pages 11-12. Applicants respectfully traverse the rejection.

The '506 patent relates to increasing the dissolution rate of nanoparticulate naproxen by including an alkali agent. This approach is different from the claimed invention and very specific for nanoparticulate compositions comprising naproxen. The '506 patent discloses that "the alkali agent functions to raise the pH of the dissolution microenvironment surrounding the naproxen, thereby increasing the dissolution rate of the naproxen composition" (column 3, lines 8-11). Accordingly, the '506 patent in view of the specification fails to render the claimed invention obvious because one skilled in the art would have understood that increasing the pH may not be effective to improve dissolution of every active agent. Accordingly, Applicants respectfully request withdrawal of the rejection.

C. **U.S. Patent No. 7,276,249**

Claims 87-106 are rejected for alleged double patenting over claims 1-177 of U.S. Patent No. 7,276,249 ("the '249 patent") and in view of Applicants' allegedly admitted prior art or Kerkhof. Applicants respectfully traverse the rejection.

For the same reasons discussed in the sections addressing the rejections under 35 U.S.C. §§ 102(b) and 103(a), the '249 patent is distinguishable from the claimed invention because it fails to disclose ***a solid dose matrix surrounding*** the nanoparticulate active agent and at least one surface stabilizer disintegrates or dissolves upon contact with saliva in less than about 3 minutes. The cited secondary reference fails to remedy the deficiencies. Therefore, the double patenting rejection over U.S. Patent No. 7,276,249 should be withdrawn.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the

undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date NOV 13, 2009

By _____

FOLEY & LARDNER LLP
Customer Number: 31049
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

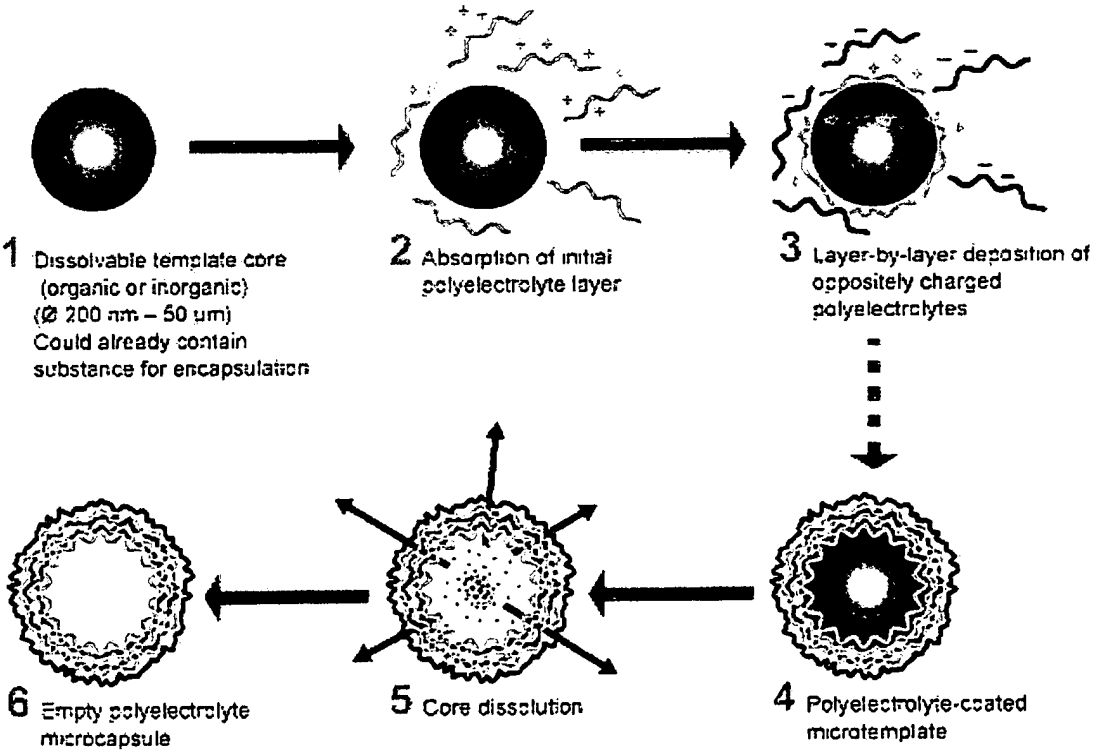
EXHIBIT A

GMD Bio Advance

TECHNOLOGY

Nanoencapsulation

Creation of nanoencapsulation shell



Colloidal particles are used for structural support.
Shell is assembled using alternating positively and negatively charged polyelectrolyte layers.
Biodegradable shells may be synthesized from polysaccharides and polypeptides.

NEXT: FINE-TUNING OF THE SHELL ▶

Atty. Dkt. No. 029318-0972

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Rajeev A. JAIN et al.

Title: RAPIDLY DISINTEGRATING SOLID ORAL DOSAGE FORM

Appl. No.: 10/667,470

Filing Date: 9/23/2003

Examiner: Brian Yong S. Kwon

Art Unit: 1614

Confirmation Number: 9048

DECLARATION UNDER 37 C.F.R. §1.132

The undersigned, Stephen B. Ruddy, hereby declares as follows:

I. Background of Stephen B. Ruddy

1. I received my Ph.D. degree in 1994 from the University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, in Pharmaceutics. I have been working in the fields of pharmaceutical drug product development, drug delivery and nanotechnology since 1992, when I joined Sterling Winthrop Pharmaceuticals Research Division, which later became Elan Drug Delivery, Inc.

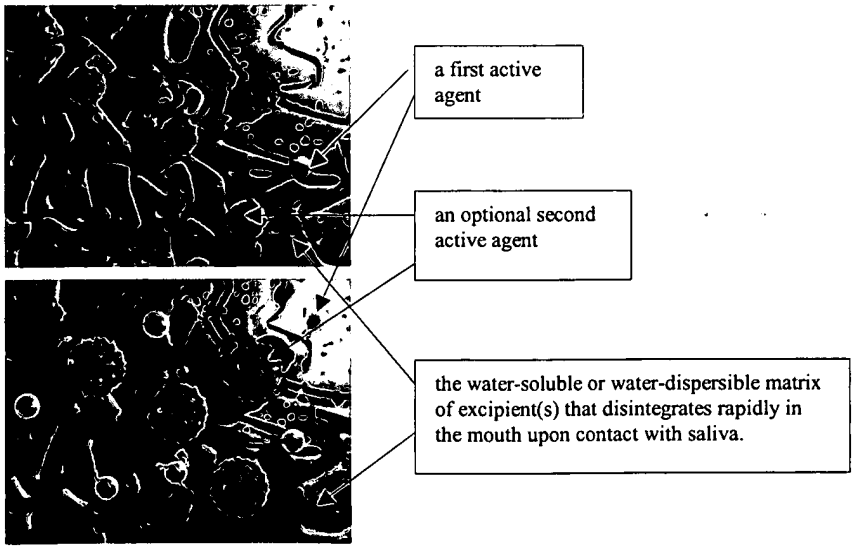
2. Currently I am a Senior Director of NanoCrystal Technology Product Development at Elan Drug Delivery, Inc., with offices at 3500 Horizon Drive, King of Prussia, PA 19406.

3. Intellectual property developed at Elan Drug Delivery, Inc. is owned by Elan Pharma International Limited., which is the assignee of the above-referenced patent application.

II. Characteristics of the Rapidly Disintegrating Solid Oral Dosage Form

4. The oral dosage forms of the claimed invention have the dual properties of: (i) rapid presentation of the poorly soluble active agent particles resulting from rapid disintegration of the solid dose matrix surrounding the active agent; and (ii) potential for rapid uptake of the poorly soluble active agent, i.e., rapid dissolution and absorption of the poorly soluble active agent obtained as a result of a stable, nanoparticulate active agent composition.

5. The claimed dosage form comprises a solid dose matrix surrounding the nanoparticulate active agent, which is stabilized by at least one surface stabilizer. The solid dose matrix comprises at least one pharmaceutically acceptable water-soluble or water-dispersible excipient such that the matrix is anticipated to disintegrate or dissolve upon contact with saliva in less than 3 minutes. The solid dose matrix is illustrated in Exhibit A, at page 5. An excerpt of the diagram is provided below, with added annotations:



6. As demonstrated in the working examples of the specification, the solid dose matrix contains pharmaceutically acceptable water-soluble and/or water-dispersible excipients. The excipients forming the solid dose matrix can rapidly hydrate and dissolve (e.g., mannitol) or

swell (e.g., croscarmellose) upon contact with saliva, thereby resulting in rapid disintegration of the solid dosage form.

Working Example	Active Agent	Surface Stabilizer	Excipient(s) Used For Solid Dose Matrix
Example 1	Compound A	hydroxypropyl cellulose (HPC-SL) and sodium lauryl sulfate (SLS)	croscarmellose sodium
Examples 3 and 4	ketoprofen	polyvinyl pyrrolidione (PVP) and sodium lauryl sulfate (SLS)	mannitol
Examples 5, 7, 8 and 10	ketoprofen	polyvinyl pyrrolidione (PVP) and sodium lauryl sulfate (SLS)	mannitol and croscarmellose sodium
Example 12	naproxen	hydroxypropyl cellulose (HPC)	lactose, mannitol and croscarmellose sodium
Example 15	Compound B	hydroxypropylmethyl cellulose (HPMC) and docusate sodium (DOSS)	lactose, mannitol and croscarmellose sodium

7. The solid dosage form exemplified in Examples 13 and 14 contained other pharmaceutical excipients, such as effervescent agents, *e.g.*, citric acid and sodium bicarbonate. Upon contact with saliva, citric acid and sodium bicarbonate can dissolve and react chemically to produce carbon dioxide gas. The attendant "foaming" or "fizzing" action subjects the tablet matrix to mechanical stress, resulting in the formation of physical defects and overall disruption of the matrix structure. The end result is rapid disintegration of the solid dosage form.

CONCLUSION

8. I declare that the statements made herein of my knowledge are true and all statements on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therein.

Stephen B. Ruddy

11 November 2009

Date

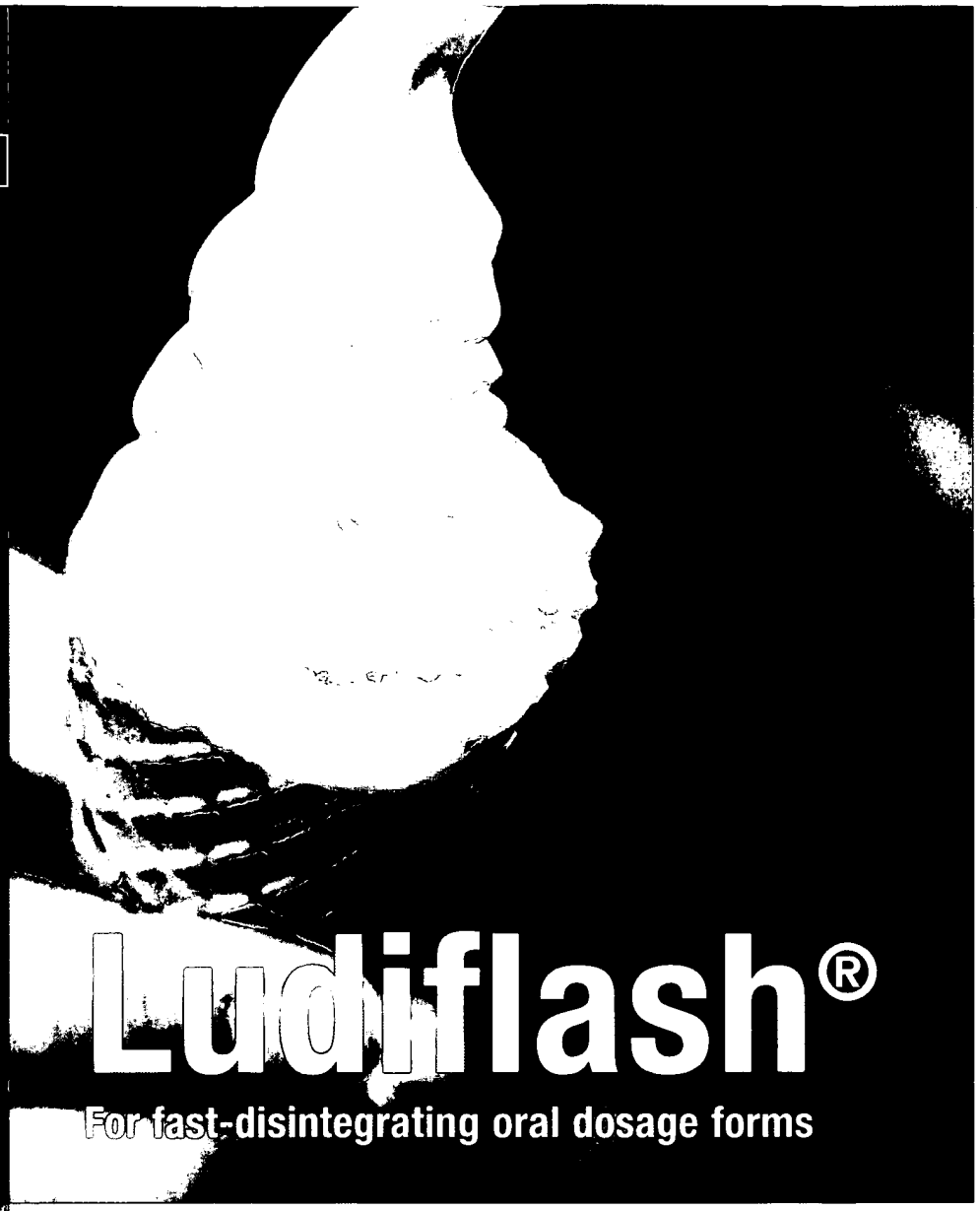
EXHIBIT A

Pharma Solutions

Custom Synthesis

Excipients

Active Ingredients



Ludiflash®

For fast-disintegrating oral dosage forms

"A tablet that melts in the mouth, with a smooth and creamy texture…"

BASF

The Chemical Company

Dr. Ralf Widmaier,
an enabler in excipients

"...and does everything else a tablet should these days."

Dr. Ralf Widmaier may just have missed his calling. As the Ludiflash product manager, he and his team are preoccupied with getting tablets to melt in the mouth – with a soft and creamy texture. So he could have made it big in the ice-cream business. But he also has other things on his mind: for example, ensuring tablets disintegrate rapidly. And are easy to manufacture. Which makes Ludiflash his pride and joy.

Some things are hard to swallow.

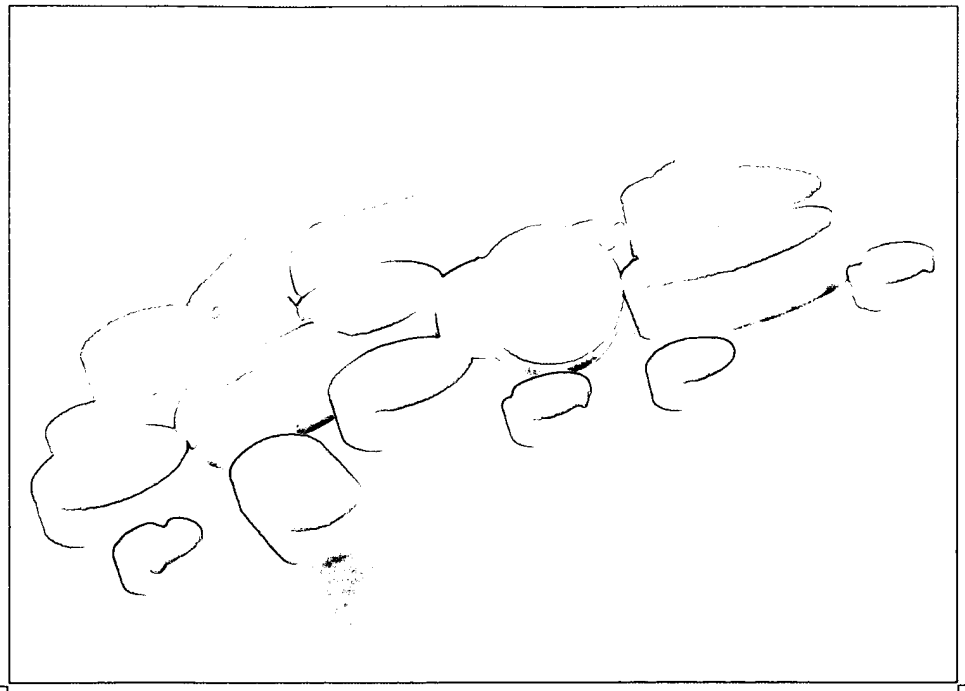
What do you do if a tablet is simply too big? Or you don't have a glass of water at hand? Or you would like to take your medication without drawing attention to yourself? More and more people – and not just children and seniors – want tablets that don't need to be swallowed. Demand is growing for products that disintegrate in the mouth within seconds, quickly releasing the active ingredients for rapid relief. That is precisely how Ludiflash works – and with a smoother, creamier texture than any other excipient to date.

As a manufacturer, you're looking for the perfect combination.

As a maker of tablets, you need flowability, compressibility, hardness and stability – guaranteeing your products are suitable for polyethylene containers and push-through blisters. In fact, on all of these scores, Ludiflash will exceed anything you have experienced.

Do business your way, with Ludiflash.

No license. No confidentiality agreement. No royalty. You are free to use your own production facilities. And retain full control over your formulation, the manufacturing process, and your expertise. Reap the benefits of full commercial independence and complete flexibility. You can focus on managing your own costs, and are not tied to someone else's. And your product and intellectual property stay where they belong – within your organization.



"Ludiflash is designed to be better than anything the market has seen to date – with regard to product properties, ease of manufacture, and consumer acceptance."

Ralf Widmaier and his team have created an excipient that provides exceptional properties throughout the entire tablet life cycle: in terms of formulation, manufacture, packaging, ingestion. And, of course, action.

Ludiflash is composed of the following:

90% Mannitol

Fast-dissolving filler with a mildly sweet taste

5% Kollidon® CL-SF (Crospovidone)

A superior tablet disintegrant:

- Highly effective, disintegrates the tablet in the presence of very little liquid
- Offers a pleasantly smooth and creamy mouthfeel

5% Kollicoat® SR 30D (Polyvinyl acetate)

Hydrophobic binder for enhanced disintegration

Ludiflash components comply with leading pharmacopoeia monographs.

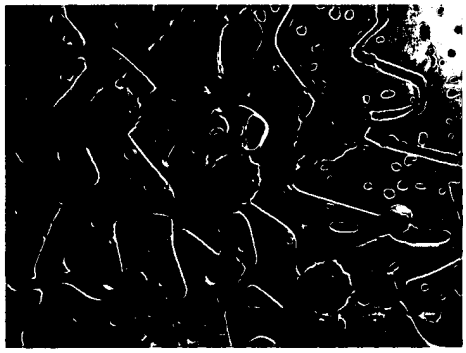
The ingredients fulfill the following requirements:
Mannitol: EP, USP, JP
Kollidon CL-SF: EP, USP, JPE
Kollicoat SR 30D: EP
An active US-drug master file is available for Kollicoat SR 30D (US-DMF no. 15055, type IV) and Ludiflash (US-DMF no. 20960, type IV).
Ludiflash is manufactured in accordance with cGMP-guidelines.
As a result, Ludiflash means quality

Ludiflash is your excipient of choice if you are looking for a fast-disintegrating, fast-acting formulation.

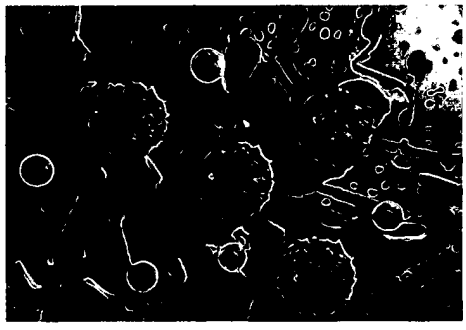
With Ludiflash, a hard tablet disintegrates ...

... in the mouth without the need for additional liquid. Within seconds ...

... it disintegrates completely to form a fine cream.



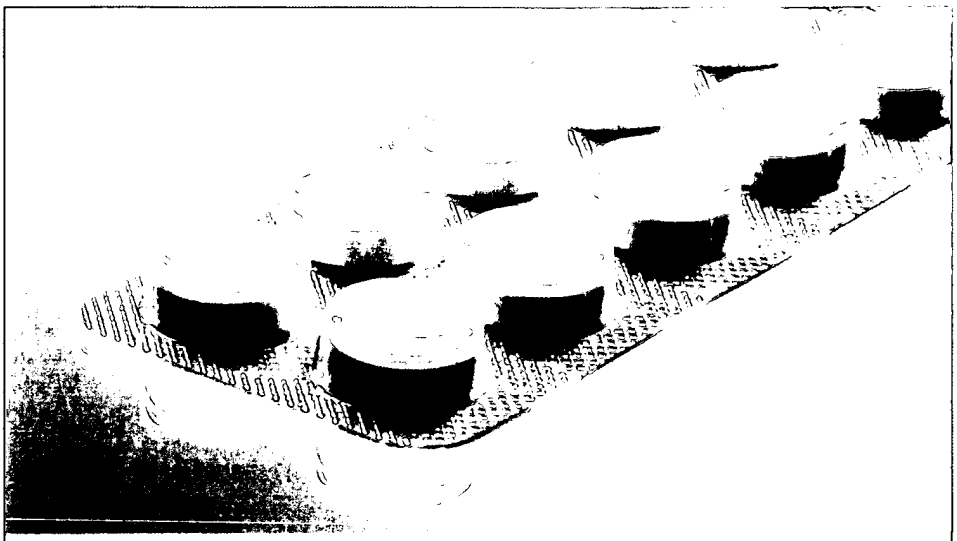
The highly porous tablet disintegrates very quickly ...



... releasing the active pharmaceutical ingredients

A unique manufacturing process gives Ludiflash exceptional properties – making Ludiflash more than just the sum of its individual, high-quality ingredients:

- Carefully controlled particle size distribution, particle structure and high bulk density combine to provide good flowability.
- A standard tableting process yields excellent content uniformity, even at high tableting speeds.
- Compact, but highly porous and fast-disintegrating tablets offer exceptional hardness and low friability.
- Tablets can be manufactured, handled and packed using standard equipment.
- Low hygroscopicity when stored as a pure powder or in finished formulations, ensures the stability of the active ingredients and of the tablet itself.



"Tableting needs to be simple, and should be possible with any conventional equipment, and with any preferred packaging type."

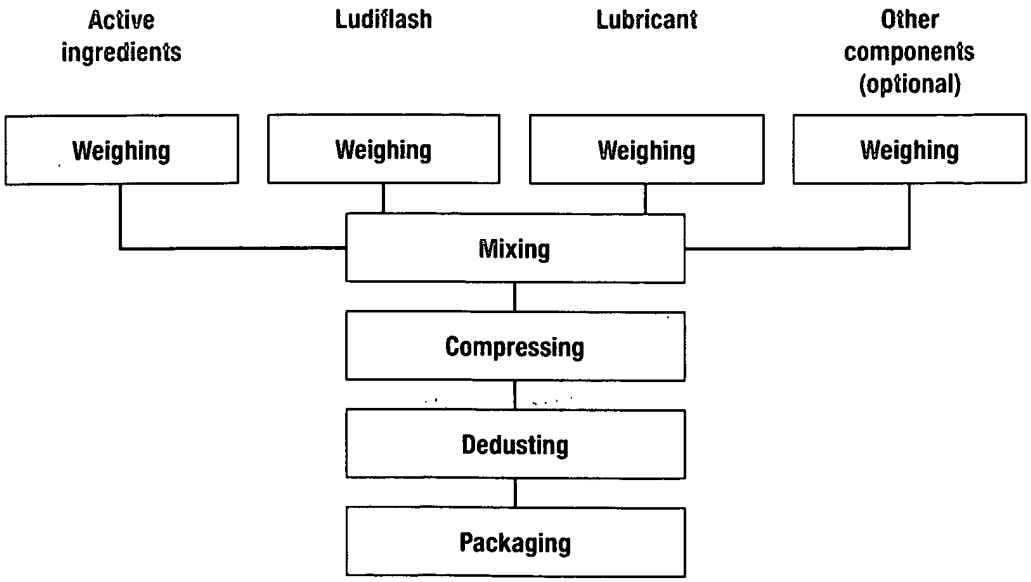
Ludiflash offers you license-free manufacturing for complete commercial independence. But it also offers you exceptional flexibility as an excipient. Ludiflash is extremely versatile, and is compatible with all conventional production equipment. It also gives you stability and hardness when and where you need it – for example, for tablets to be packaged in PE-containers or push-through blisters.

Ludiflash saves you time, money and headaches.

Ludiflash is suitable for direct compression and roller compaction. It can also be used in wet-granulation processes, where required by the active ingredient, or for other reasons. The blends can be processed on standard tableting machines, or used in the form of granulate or powder. Ludiflash offers good flowability, minimal water absorption, exceptionally high cohesion, and no segregation of the active ingredients. As a result, it can be easily processed.

Direct compression offers clear advantages: The components are weighed, mixed and directly compressed. What's more, direct compression is very gentle on the active ingredients.

With Ludiflash, you can manufacture tablets in high quality at low cost – and with short time-to-production.



Ludiflash tablets can be packed in push-through blisters, polyethylene containers, sachets and more – using standard equipment. To ensure excellent long-term stability across all humidity ranges, BASF recommends the

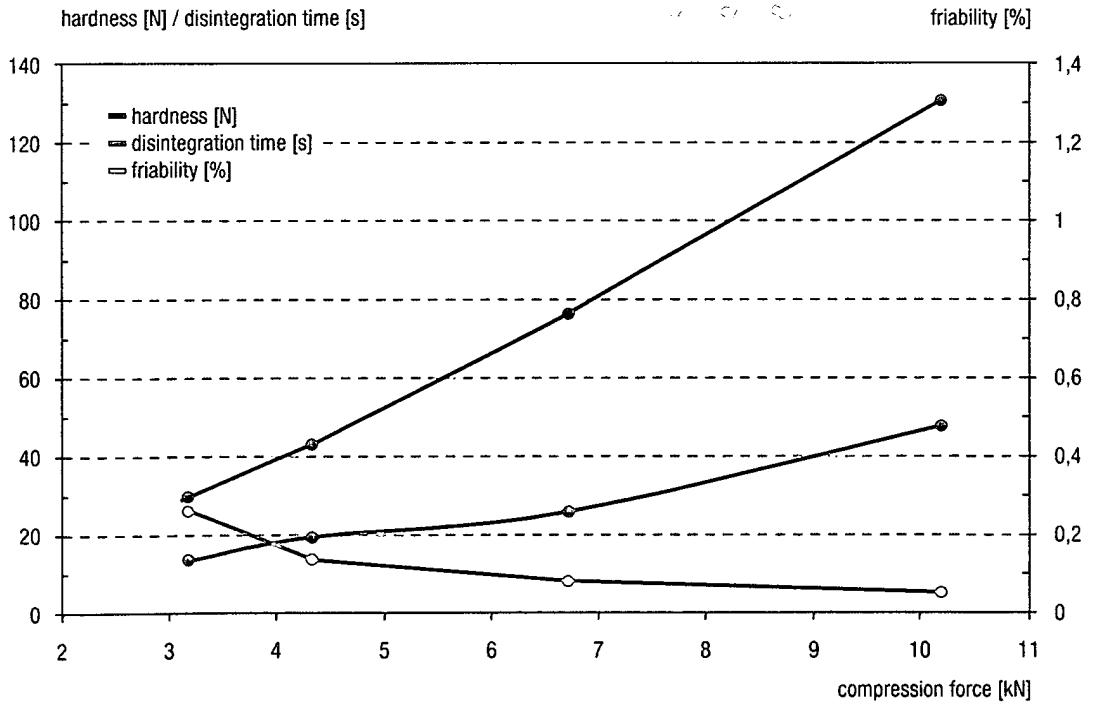
"It's designed to create a uniquely pleasant mouthfeel: it disintegrates to form a smooth, creamy texture like no other excipient to date."

Consumers want a pleasant-tasting, fast-acting tablet that can be taken anywhere, anytime – without the need for water. They want a tablet that completely disintegrates within moments, with no bitterness or chalky aftertaste. With Ludiflash, that is exactly what they get.

Example application: a Ludiflash-based placebo

With Ludiflash, you can manufacture tablets that are extremely hard, yet disintegrate in seconds.

The tablets also exhibit low friability, and have an especially pleasant mouthfeel.



FORMULATION	
▫ Ludiflash	294.0 mg
▫ Natrium stearyl fumarate	6.0 mg
▫ Total weight	300.0 mg

TABLET PROPERTIES	
▫ Weight	300.0 mg
▫ Form	10 mm flat
▫ Hardness	44 N
▫ Friability	< 0.2 %
▫ Disintegration time (phosphate buffer pH 7.2)	19 s
▫ Disintegration in the oral cavity	ca. 15 s
▫ Taste	extremely pleasant mouthfeel

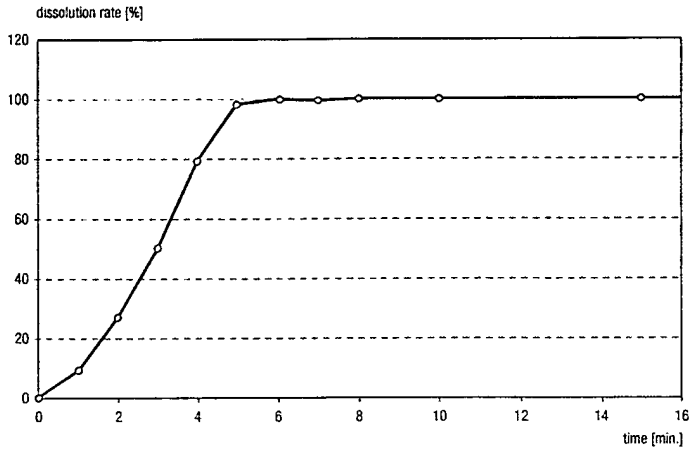
PRODUCTION PROCESS

All ingredients are blended in a free-fall mixer for 10 minutes, passed through an 0.8 mm sieve and compressed at a force of 4.8 kN using a Korsch XL-series press.

Example application: Risperidone formulation with Ludiflash

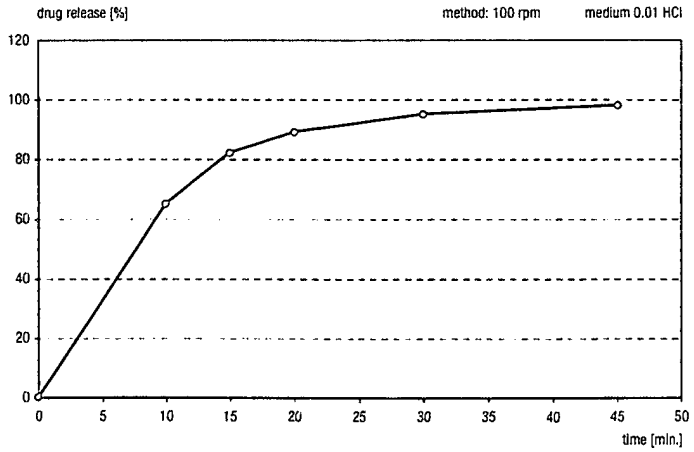
With Ludiflash, the Risperidone formulation exhibits a hardness of 56 N and an extraordinarily low friability of under 0.1% at a compression force of only 4 kN.

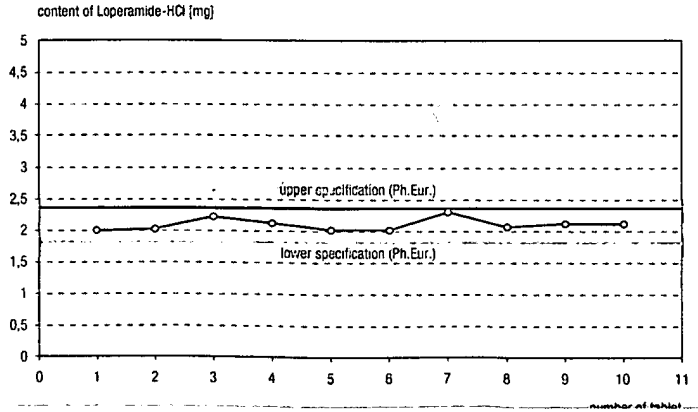
The disintegration time is less than 30 seconds and 98% of the active ingredients are released within only 5 minutes.



Example application: Loperamide formulation with Ludiflash, and additional Kollidon® CL-SF

With the Loperamide formulation, it is possible to achieve a hardness of 30 N at a compression force of only 3.7 kN, and an extraordinarily low friability of less than 0.1%. The tablet disintegrates completely within only 11 seconds, and releases 95% of the active ingredients within 30 minutes. Tablet uniformity is achieved with an extremely high degree of reliability.





FORMULATION	
▫ Risperidone	1.0 mg
▫ Ludiflash	96.0 mg
▫ Aerosil® 200	0.5 mg
▫ Lemon powder	0.5 mg
▫ Aspartame	1.0 mg
▫ Magnesium stearate	1.0 mg
▫ Total weight	100.0 mg

PRODUCTION PROCESS

The ingredients are blended in a free-fall mixer for 10 minutes, passed through an 0.8 mm sieve and compressed at a force of 4 kN at 40 rpm.

TABLET PROPERTIES	
▫ Weight	100.0 mg
▫ Form	6.5 mm
▫ Hardness	56 N
▫ Friability	< 0.1 %
▫ Disintegration time (water)	27 s
▫ Release rate (water, 900 ml, 50 rpm)	98.2 % (5 min.)

CONTENT UNIFORMITY (N-10)

- Mean = 98.8 %
- Maximum = 102.1 %
- Minimum = 97.7 %
- Standard deviation = 2.2

Thanks to its unique composition and manufacturing process, Ludiflash produces tablets with:

- An excellent compression/hardness curve
- Very low friability
- Very high content uniformity
- Excellent mass uniformity

Ludiflash is the excipient of choice for fast-disintegrating formulations for rapid relief. **It is compatible with other typical ingredients in standard formulations.**

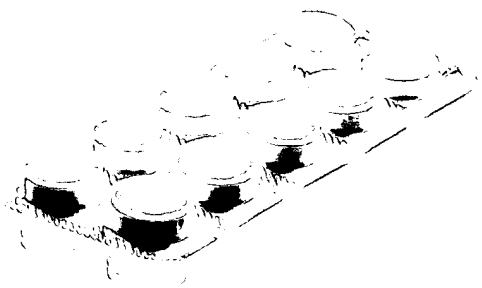
Adding small amounts of BASF's **Kollidon® CL-SF** further accelerates disintegration. This allows the disintegration time to be reduced without compromising the smooth and creamy mouthfeel of Ludiflash. With its exceptionally high swelling volume and swelling pressure, Kollidon CL-SF (Crospovidone) ensures that even tablets of superior hardness disintegrate within seconds.

FORMULATION	
▫ Loperamide HCl	2.0 mg
▫ Ludiflash	94.5 mg
▫ Kollidon CL-SF	1.0 mg
▫ Chocolate flavoring	1.5 mg
▫ Sodium stearyl fumarate	1.0 mg
▫ Total weight	100.0 mg

PRODUCTION PROCESS

The ingredients are blended in a free-fall mixer for 10 minutes, passed through an 0.8 mm sieve and compressed at a force of 3.7 kN.

TABLET PROPERTIES	
▫ Weight	100.0 mg
▫ Form	7 mm, concave
▫ Hardness	30 N
▫ Friability	0.09 %
▫ Disintegration time (phosphate buffer pH 7.2)	11 s
▫ Release rate (0.01 N HCl/100 rpm)	94.7 % (30 min.)



"In a nutshell, here's what Ludiflash can do for you."

If you want to manufacture a tablet that dissolves directly in the mouth, without the need for water, Ludiflash is the answer – for more reasons than one:

Ludiflash cuts your costs

- ☐ All-in-one system: filler, binder and disintegrant
- ☐ Lower storage costs (one material, not three)
- ☐ Lower analysis costs
- ☐ Faster product development, and faster process validation

Ludiflash can enhance the properties of your tablets

- ☐ Tablets with exceptional tensile strength and hardness
- ☐ Tablets with extremely low friability
- ☐ Minimal hygroscopicity
- ☐ Extremely rapid disintegration
- ☐ Extremely fast release rate
- ☐ Packaging possible in suitable push-through blisters and PE containers

Ludiflash can simplify your tableting process

- ☐ Good flowability
- ☐ No segregation of active ingredients
- ☐ High compression speeds without compromising tensile strength
- ☐ Low-cost, high-speed manufacture

Ludiflash gives you independence

- ☐ No license, no confidentiality, no royalty: full control over formulation, manufacturing process and intellectual property

Ludiflash makes for a more pleasant consumer experience

- ☐ Disintegrates in the mouth within seconds
- ☐ Creamy and smooth mouthfeel
- ☐ Easy-to-use: mechanically stable tablets in push-through blisters
- ☐ Neutral to mildly sweet, pleasant taste
- ☐ Sugar-free, non-cariogenic ingredients
- ☐ Can be taken without water – anywhere, anytime
- ☐ Fast acting for rapid relief: promotes patient compliance

Ludiflash is practically in a league of its own when it comes to excipients for direct-compression tablets that rapidly disintegrate in the mouth to form a smooth and creamy texture.

Take advantage of the unique properties of Ludiflash.

"BASF experts around the world can enable your business to gain competitive advantage. Why not take a closer look?"

- **ExAct Magazine**
  Active ingredients, excipients and intermediate products from BASF can be found in most pharmaceutical dosage forms, whether tablets, capsules, liquids, sprays, injectable solutions or gels. ExAct keeps you up to speed on our comprehensive range of products and services for the pharmaceutical industry.

- **Kollicoat® Grades**
  For all manufacturers of solid dosage forms. This guide describes in detail the seven grades of Kollicoat coating available. Includes information on the controlled release of active ingredients. Also provides numerous example applications and an entire chapter on trouble-shooting.

- **Kollidon®**
  For anyone working in the manufacture and quality control of pharmaceuticals. Provides an extensive overview of product properties of povidone, copovidone and crospovidone, formulations of active ingredients, manufacturing techniques, dosage forms and analytical techniques.

- **Generic Drug Formulations**
  The right formulation is vital to creating fast-acting, reliable medication. More than 500 BASF formulations for solid, semi-solid and liquid dosage forms are available on CD-ROM or at: www.pharma-solutions.basf.com

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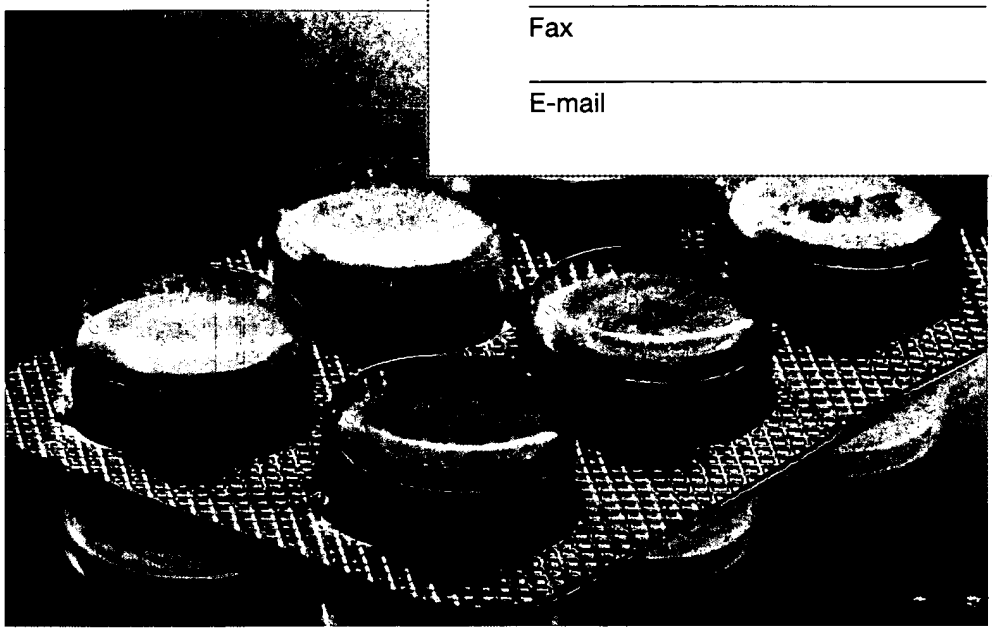

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Please complete the form and fax to us.
Alternatively, simply detach the postcard and mail it to us.

Please provide me with the following information.

- ☐ Technical information on Ludiflash®
- ☐ Sample of Ludiflash 1 kg
- ☐ Please contact me – I would like to know more about Ludiflash
- ☐ Technical information on the Kollicoat® product(s) _____
- ☐ Technical information on the Kollidon® product(s) _____
- ☐ Technical information on the Ludipress® product line
- ☐ ExAct magazines (Excipients & Active Ingredients for Pharma)

Please complete and fax this form to your BASF representative, regional office (see reverse for list) or to our headquarters in Germany:

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BASF experts around the world can make things happen for you, too.

Simply get in touch with your local BASF representative or contact one of our regional offices.

We look forward to hearing from you, and are happy to answer any questions you might have.

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  BASF offers custom synthesis services – producing active ingredients and intermediate products for pharmaceutical companies on an exclusive basis, and in the strictest confidence. Our experts provide advice and assistance throughout the entire life cycle.

- **Excipients**
  Kollidon® grades – A group of Povidone and Copovidone products, primarily used as tablet binders. Crospovidone is also ideal as a tablet disintegrant and dissolution enhancer.
  Kollidon® SR – matrix sustained release polymer.
  Kollicoat® grades – range of aqueous-based film formers, cost-efficient and eco-friendly.
  Ludipress® grades – direct tableting aids for faster product development and rapid processing.
  Lutrol® grades – range of PEGs (Lutrol E) and poloxamers (Lutrol F) for a wide variety of pharmaceutical dosage forms.
  Soluphor® P – 2-pyrrolidone.
  Cremophor® grades and Solutol® HS 15 – range of ethoxylated emulsifiers and solubilizers suitable for topical, oral and parenteral formulations.

- **Selected Active Ingredients**
  Aminophyllin
  Benoxinate (Oxybuprocaine) HCl
  Benzonatate
  Bethanechol Chloride
  Bupivacaine Base and HCl
  Caffeine
  Carticaine (Articaine) HCl
  Cathin
  Dexpanthenol
  Diprophyllin
  Dobutamine
  Dopamine
  Ephedrine
  Ibuprofen
  Isotretinoin
  Methylphenidate HCl
  Oxybutynin Base and HCl
  Oxymetazoline
  Pseudoephedrine
  PVP-Iodine
  Ribavirin
  Tetracaine Base and HCl
  Theophylline
  Tretinoin
  Tricaine Methanesulfonate
  Selegiline
  Vitamins
  Xylometazoline

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